



1614/2006

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

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|-------------|--|---|------------------|------------------|
| Applicant: | Wilfried Lubisch et al. |) | Examiner: | Unknown |
| Serial No.: | 10/582,285 |) | Group Art Unit: | Unknown |
| Filed: | 06/09/2006 |) | Confirmation No. | |
| For: | Keto Lactam Compounds and Use Thereof |) | Atty. Dkt.: | ABB10010P02230US |

TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Enclosed please find the English translation of the International Preliminary Report on Patentability and Written Opinion of the International Searching Authority issued in the PCT application (PCT/EP2004/014118) of this National Phase application. Applicants respectfully request the aforementioned documents be entered into the official record of the above-captioned application.

Respectfully submitted

By Martin L. Katz
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CERTIFICATE OF MAILING

I hereby certify that this correspondence and enclosures are being deposited with the United States Postal Service with sufficient postage at First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on **October 4, 2006**

Stephanie Frain
Stephanie Frain

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44bis.3(c) and 72.2)

To:

REITSTÖTTER - KINZEBACH
Reitstötter, Kinzebach & Partner (GmbH)
Ludwigsplatz 4
67059 Ludwigshafen
ALLEMAGNE

Patentanwälte
Reitstötter, Kinzebach & Part.

Eing. 13. Sep. 2006

Ludwigsplatz 4, D-67059 Ludwigshafen

Date of mailing (day/month/year)
08 September 2006 (08.09.2006)

Applicant's or agent's file reference
M/43136-PCT

IMPORTANT NOTIFICATION

International application No.
PCT/EP2004/014118

International filing date (day/month/year)
10 December 2004 (10.12.2004)

Applicant

ABBOTT GMBH & CO. KG et al

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer:

Ellen Moyse

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | | |
|--|---|---|------------------|
| Applicant's or agent's file reference M/43136-PCT | FOR FURTHER ACTION | | See item 4 below |
| International application No. PCT/EP2004/014118 | International filing date (day/month/year) 10 December 2004 (10.12.2004) | Priority date (day/month/year) 11 December 2003 (11.12.2003) | |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | | |
| Applicant ABBOTT GMBH & CO. KG | | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input type="checkbox"/> Box No. II | Priority |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70 | Date of issuance of this report 29 August 2006 (29.08.2006) |
| | Authorized officer Ellen Moyse e-mail: pt05@wipo.int |

PATENT COOPERATION TREATY

TRANSLATION

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

Date of mailing
(day/month/year)

See form PCT/ISA/210

Applicant's or agent's file reference

M/43136-PCT

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/EP2004/014118

International filing date (day/month/year)

10.12.2004

Priority date (day/month/year)

11.12.2003

International Patent Classification (IPC) or both national classification and IPC

C07D403/12, C07D401/12, C07D223/16, A61K31/55, A61P13/12,
A61P25/28

Applicant

ABBOTT GMBH & CO. KG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/014118

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐

This opinion has been established on the basis of a translation from the original language into the following language

_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 25.1(h)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☐

in written format

☐

in computer readable form

c. time of filing/furnishing

☐

contained in the international application as filed

☐

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority for the purposes of search.

3. ☐

In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/014118

Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 1-28 (in part)

because:

- ☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (specify):

- ☐ the description, claims or drawings (indicate particular elements below) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (specify):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 1-28 (in part)

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☒ See Supplemental Box for further details.

| WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY | | International application No. PCT/EP2004/014118 |
|---|---|--|
| Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement | |
| 1. Statement | | |
| Novelty (N) | Claims <u>1-28</u> | YES |
| | Claims _____ | NO |
| Inventive step (IS) | Claims _____ | YES |
| | Claims <u>1-28</u> | NO |
| Industrial applicability (IA) | Claims <u>1-28</u> | YES |
| | Claims _____ | NO |
| 2. Citations and explanations: | | |
| <p>1 The present application is concerned with ketolactam compounds which can be used as dopamine D3 receptor modulators in the case of disorders of the central nervous system and in the case of kidney malfunctions. What is claimed is some of these compounds (independent claim 1), pharmaceutical preparations containing them (independent claim 25) and the use of the said compounds for producing pharmaceutical preparations (independent claim 26).</p> | | |
| <p>2 Reference is made to the following documents. The same numbering of the documents will be used throughout the procedure:</p> <p>D1: ORJALES A ET AL., EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 37, no. 9, September 2002, pages 721-730</p> <p>D2: WO 97/25324 A (BASF AKTIENGESELLSCHAFT; TREIBER, HANS-JOERG; BLANK, STEFAN; STARCK, D) 17 July 1997</p> <p>D3: HACKLING A E ET AL., CHEMBIOCHEM - A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY, WILEY VCH, WEINHEIM, DE, vol. 3, no. 10, 4 October 2002, pages 946-961</p> <p>D4: WO 00/76981 A (NEUROGEN CORPORATION; ZHAO, HE; THURKAUF, ANDREW) 21 December 2000</p> <p>D5: LEOPOLDO M ET AL., JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 45,</p> | | |

| WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY | | International application No. PCT/EP2004/014118 |
|---|---|--|
| Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement | |
| no. 26, 22 November 2002, pages 5727-5735 | | |
| 3 | <p>D1 discloses the two structurally closest compounds 20 and 28, but these do not come within the claim range searched since the bicycle there (with Z) is different from the corresponding substituent Ar of the present formula (I) or (I'). The present claims are therefore novel (PCT Article 33(2)).</p> | |
| 4 | <p>The present claims are not inventive within the meaning of PCT Article 33(3):</p> <p>D₁ modulators of the ring-spacer-piperazine-bond/spacer-aromatic type are known from the prior art (see D2, D3, D5). The present technical problem appears, in view of, for example, D2 as most relevant prior art, to provide alternative selective D₃ modulators. Starting out from the basic structure of the above ligand type, the present technical solution is variation of the "ring" which in the present case is a bicyclic azepinedione derivative or a compound similar thereto.</p> <p>D1 discloses dopamine modulators which contain the heterocycles 1-10 and can thus, according to D1, be expected to display dopamine activity. Mention is made of, <i>inter alia</i>, the compounds 20 and 28 and further structurally similar compounds which have a "ring" as in the compounds claimed. Since these compounds have a low activity compared to D₃, a person skilled in the art seeking dopamine modulators of the D₃ group which selectively bind to D₃ rather than D₂ would consider an appropriate variation of the "ring" starting out from known modulators of the ring-spacer-piperazine-bond/spacer-aromatic type. The subject matter of claims 1-26 therefore does not appear to be inventive.</p> | |

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/014118

| | |
|-----------|---|
| Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement |
|-----------|---|

- 5 The present claims are industrially applicable and meet the requirements of PCT Article 33(4).

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/014113

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box III

The present compound claims 1-24 (and therefore also the further claims 25-28) relate in part to a disproportionately large number of possible compounds of which only a small proportion is supported by the description within the meaning of PCT Article 6 and/or can be considered to be disclosed in the patent application within the meaning of PCT Article 5. In the present case, the claims lack the proper support and the application lacks the requisite disclosure to such an extent that it does not appear possible to carry out a meaningful search covering the entire range of protection sought.

The search was therefore directed to the parts of the claims which appear to be supported and disclosed in the above sense, namely claim 1 in combination with claims 2, 3, 4, 6 and 9, i.e. in the present formulae (I), (I'), (I-Aa), (I-A'a) and (I-Ba), the respective restrictions of the said dependent claims were taken over for the variables group R^x, R^y (claim 2), D (claim 3), A (claim 4), N ring (claim 6) and R^z (claim 9).